Claims

1. (Currently Amended) A method of modifying a target nucleic acid of interest at a target locus within a genome, comprising:

a) introducing into a host cell a gene targeting construct (GTC) by transformation of the host cell *in vitro* with a DNA comprising a nucleic acid sequence encoding the GTC, and culturing the host cell or transformed progeny of the host cell so as to:

i) express a gene targeting message RNA from the GTC, wherein the message RNA ~~is capable of self-priming~~ self-primes reverse transcription by a reverse transcriptase (RT) expressed by the host cell or the transformed progeny of the host cell;

ii) wherein at least a portion of the gene targeting message RNA is reverse transcribed to produce a gene targeting substrate (GTS) having a gene targeting nucleotide sequence (GTNS), wherein the GTNS is homologous to the target locus and comprises a sequence modification compared to the target nucleic acid;

iii) wherein the GTNS mediates insertion, deletion or substitution of one or more bases of the sequence of the target nucleic acid to produce a sequence modification at the target locus within the genome; and,

b) selecting a host cell or transformed progeny of the host cell having the sequence modification at the target locus.

2. (Withdrawn) The method of claim 1, wherein the host cell is capable of expressing the RT prior to transforming the host cell with the gene targeting construct.

3. (Previously Presented) The method of claim 1, further comprising transforming the host cell or the transformed progeny of the host cell so as to be capable of expressing the RT.

4. (Previously Presented) The method of claim 1, wherein the GTC is introduced into the transformed progeny of the host cell by cell fusion.

5. (Cancelled)

6. (Withdrawn) The method of claim 1, wherein the gene targeting construct comprises an msr coding region encoding an msr element and an msd coding region encoding an msd element.

7. (Withdrawn) A method of claim 1, wherein the GTC comprises a recombinant reverse transcriptase coding sequence encoding the reverse transcriptase, and the RT has a nuclear localization signal sequence.

8. (Withdrawn) The method of claim 6, wherein the msr and msd coding regions are in operative association with a first regulatory region, and the construct further comprises a nucleotide sequence encoding the reverse transcriptase.

9. (Withdrawn) The method of claim 8, wherein the nucleotide sequence encoding the reverse transcriptase is in operative association with the first regulatory region or with a second regulatory region.

10. (Withdrawn) The method of claim 1, wherein the reverse transcriptase comprises a nuclear localization signal sequence.

11. (Withdrawn) The method of claim 8 wherein the first regulatory region is operatively active at a cell cycle stage in an S phase, a G2 phase, an S/G2 or a G1/S boundary of a cell cycle, or during meiosis, and wherein the reverse transcriptase is under the control of the first regulatory region or under the control of a second regulatory region that is operatively active at the same cell cycle stage as the first regulatory region.

12. (Withdrawn) The method of claim 11, wherein the first regulatory region and the second regulatory region are selected from the group consisting of a histone promoter, a cyclin promoter, a promoter associated with a gene involved in DNA replication, a promoter associated with a gene involved in DNA repair and a promoter associated with a gene involved in DNA homologous recombination.

13. (Withdrawn) The method of claim 1, wherein the gene targeting construct further comprises a nucleotide sequence encoding a selectable marker.

14. (Cancelled)

15. (Cancelled)

16. (Withdrawn) The method of claim 1, wherein the host cell is selected from the group consisting of a plant cell, an animal cell, a yeast cell, and an insect cell.

17. (Withdrawn) The method of claim 16, wherein the host cell is a plant cell.

18. (Cancelled)

19. (Cancelled)

20. (Withdrawn) The method of claim 1 wherein the host cell is a eukaryotic cell.

21. (Withdrawn) The method of claim 20, wherein the host cell is a yeast cell.

22. (Previously Presented) The method of claim 1, wherein the gene targeting nucleotide sequence comprises one, or more than one, region of 15 to about 500 nucleotides, exhibiting about 70% to about 99% sequence similarity with the target locus sequence, as determined using the following conditions: Program: blastp; Database: nr; Expect 10; filter: default; Alignment: pairwise; Query genetic Codes: Standard (1).

23. (Previously Presented) The method of claim 22, wherein the one or more than one region is of less than 300 nucleotides in length.

24. (Previously Presented) The method of claim 6, wherein the msr and msd elements comprise inverted repeat sequences b1 and b2, and are further flanked by inverted repeat sequences a1' and a2'.

25. (Previously Presented) The method of claim 24, wherein the GTNS is inserted at a unique restriction site between the inverted repeat sequences b1 and b2 of the gene targeting construct.

26. (Previously Presented) The method of claim 24, wherein the inverted repeat sequences a1' and a2' are longer than inverted repeat sequences a1 and a2 of a wild-type retron.

27. (Previously Presented) The method of claim 24, wherein the gene targeting construct further comprises two inverted repeat sequences s1 and s2 within the 5' end of the msd region, the inverted repeat sequences s1 and s2 being capable of forming a stem-and-loop structure in the gene targeting message RNA having a sufficiently high dissociation constant so as to impair progression of the reverse transcriptase there through.

28. (Previously Presented) The method of claim 24, wherein the msd element is 5' of the msr element and the inverted repeat sequences a1' and a2' are adjacent to each other between the msd and msr elements, and wherein the GTNS is inserted in a unique restriction site in the msd element 5' of the inverted repeat sequence b1.